REMARKS

Status of the Claims

Pending claims

Claims 1 to 120 as filed are pending.

Claims amended and canceled in the instant amendment

Claims 19 to 46, 49 to 73, 89, 90, 93 to 100 and 108 to 110 and 116 are canceled, without prejudice. Thus, after entry of the instant amendment, claims 1 to 18, 47, 48, 74 to 88, 91, 92, 101 to 107, 111 to 115, 117 to 120 will remain pending.

Restriction Requirement

In the Restriction Requirement mailed May 22, 2003, the Patent Office alleged that the pending claims of the application are directed to eight hundred and ninety-nine (899) separate and distinct inventions under 35 U.S.C. §121.

In response, Applicants elected Group 62, for the nucleic acid having a sequence as set forth in SEQ ID NO:125, claims 1-29, 47-48, 74-92, and 101-106, drawn to a nucleic acid having a sequence as set forth in SEQ ID NO:125, vectors, host cells, probes and a method of making the encoded polypeptide (SEQ ID NO:126), with traverse.

In their reasons to reconsider and withdraw the restriction requirement Applicants respectfully requested that Groups 34, 36-38, 41-43, 50-56, 58, 60-79, 81, and 83-105, corresponding to odd numbered SEQ ID NOS:69, 73-77, 83-87, 101-113, 117, 121-159, 163, and 167-211, be rejoined, as they are all isolated from environmental samples.

Rejoining process claims

Applicants respectfully requested that, after the elected product claims have been found to be allowable, all withdrawn process (methods) claims which depend from or otherwise include all of the limitations of the allowed product claims be rejoined. MPEP §821.04; pg 800-63, 8th Edition, August 2001; In re Ochiai, 37 USPQ2d 1127 (Fed. Cir. 1995); In re Brouwer, 37 USPQ2d 1663 (Fed. Cir. 1995); 1184 OG 86, 3/26/96.

Outstanding Rejections

Claims 2 to 4, 7 to 15, 29, 47, 74 to 91 and 103 to 106 are rejected under 35 U.S.C. §112, second paragraph. Claims 1 to 5, 16 to 29, 47, 48, 74 to 92, and 101 to 106, are rejected under 35 U.S.C. §112, first paragraph. Claims 1 to 12, 16 to 29, 47, 48, 74 to 86, 89 to 92 and 101 to 106, are rejected under 35 U.S.C. §102. Claims 87 and 88 are rejected under 35 U.S.C. §103.

Applicants respectfully traverse all outstanding rejections of the claims.

Request for Telephonic Interview

Applicants respectfully request a telephonic interview before mailing of a further office action to discuss how the instant response and amendment addresses the outstanding rejections.

Support for the Claim Amendments

Support for the new and amended claims can be found throughout the application for the skilled artisan. For example, support for claims directed to nucleic acids and polypeptides of the invention of various lengths can be found, inter alia, in paragraphs 176 to 178, pages 43 to 44, of the specification.

Issues under 35 U.S.C. §112, second paragraph

Claims 2 to 4, 7 to 15, 29, 47, 74 to 91 and 103 to 106 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention.

The terms involving stringent conditions of hybridization

The Patent Office alleges that claims are indefinite in the recitation of terms directed to various levels of "stringent conditions" of hybridization because the exact conditions defining the hybridization conditions are not set forth in the claims or the specification. The instant amendment addresses this issue.

The phrase "sequences complementary to ...."

The Patent Office alleges that claims are indefinite in the recitation of terms including "sequences complementary to ...." as described on page 4, lines 4 to 15, of the instant office action. The instant amendment addresses this issue.

The term "fosmid"

Applicants respectfully note that a fosmid is, and at the time of the invention was, a known type of vector. For example, please see the attachment of Appendix A.

The phrase "metabolically rich hosts"

The Patent Office alleges that the phrase "metabolically rich hosts" is indefinite. The instant amendment addresses this issue.

In light of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims based upon 35 U.S.C. §112, second paragraph.

Issues under 35 U.S.C. §112, first paragraph

Claims 1 to 5, 16 to 29, 47, 48, 74 to 92, and 101 to 106, are rejected under 35 U.S.C. §112, first paragraph.

Written Description

The Patent Office alleges that the specification does not contain any disclosure of the structure and function of the genus of polynucleotides encoding alpha amylases which comprise a sequence which hybridizes to SEQ ID NO:125 under stringent conditions or to nucleic acids having a percent sequence identity to SEQ ID NO:125. It is alleged that claims directed to a genus of polynucleotides are not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention.

To address the Examiner's concerns, Applicants have amended the appropriate claims to be directed to nucleic acids encoding alpha amylases having at least 85% sequence identity to SEQ ID NO:125, or, the appropriate claims are amended to include specific

hybridization conditions. Specifically, a wash step has been added to clearly define the stringency of the hybridization conditions.

In light of these amendments, Applicants respectfully submit that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Applicants respectfully aver that describing a genus of polynucleotides in terms of its physico-chemical properties (e.g., stringent hybridization conditions, including a wash step) and function (e.g., nucleic acids having at least 85% identity to SEQ ID NO:125 encoding a polypeptide having alpha amylase activity) satisfies the written description requirement of section 112, first paragraph.

Applicants respectfully aver that a single species of the instant invention is sufficient to put one of skill on the art in possession of the claimed genus. Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph. In example 14 of the guidelines (a copy of which is attached as Exhibit B), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the genus of nucleic acids of the claimed invention is described by structure (the exemplary nucleic acid), a physico-chemical property (percent sequence identity or stringent hybridization conditions) and function (having amylase activity). All nucleic acids of the genus used in the claimed methods must have a percent sequence identity to an exemplary

sequence of the invention (or, hybridize under specific conditions to an exemplary sequence of the invention). The USPTO guidelines recognize that written description is met for a genus of polypeptides described by structure, a physico-chemical property (e.g., a % sequence identity, hybridization under specific conditions) and a defined function (e.g., amylase activity), the genus of claimed polypeptides also meet the written description requirements of section 112.

The genus of nucleic acids of the claimed invention also fully comply with the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of the claimed amylase-encoding nucleic acids. The claimed genus of polypeptides all must have amylase activity and a specific physical characteristic, e.g., a % sequence identity to the exemplary nucleic acid, or, hybridization under specific conditions to an exemplary sequence of the invention. Therefore, the genus of nucleic acids used in the claimed methods is defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

More recently, the Federal Circuit stated

> Similarly, in this court's most recent pronouncement, it noted:
>
> > More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.
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> Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the function of the amylases encoded by the nucleic acids of the invention is sufficiently correlated to a particular, known structure (the exemplary sequences) and a physical (physico-chemical) property (percent sequence identity or specific hybridization conditions). Accordingly, the sequences used in the claimed methods are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Applicants also respectfully refer to recently issued claims directed to genuses of polynucleotides based on sequence identity (and stringent hybridization) to an exemplary nucleic acid, see, e.g., recently issued claims directed to, e.g., 72.5% sequence identity, as in USPN 6,593,514 (July 15, 2003); 75% sequence identity (and "stringent hybridization"), as in USPN 6,586,215 (July 1, 2003); 80% sequence identity, as in USPN 6,680,185 (January 20, 2004), USPN 6,676,943 (January 13, 2004); USPN 6,677,145 (January 13, 2004), USPN 6,677,502 (January 13, 2004) and USPN 6,596,926 (July 22, 2003); 85% sequence identity, as in USPN 6,590,141 (July 8, 2003) and USPN 6,586,179; 86% sequence identity, as in USPN 6,583,337 (June 24, 2003); and, 90% sequence identity, as in USPN 6,689,352 (February 10, 2004) (see Exhibit B).

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are sufficiently described in the specification to overcome the 35 U.S.C. §112, first paragraph, rejection.

Enablement

Claims 1 to 5, 16 to 29, 47, 48, 74 to 92, and 101 to 106 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

The Patent Office notes that the specification enables polynucleotides encoding SEQ ID NO:126. However, it is alleged that the specification does not reasonably provide enablement for the claimed genus of nucleic acids.

As discussed above, Applicants believe that entry of the instant amendments addresses the Examiner's concerns. Applicants have amended the appropriate claims to add the limitation that nucleic acids having at least 85% identity to SEQ ID NO:125 encode a polypeptide having alpha amylase activity. Claims incorporating hybridization conditions limitations have been amended to add the limitation of a wash step.

The Patent Office alleged that it is not routine experimentation to screen for multiple substitutions or multiple modifications as encompassed by the claims. It is alleged that it would have required some knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with amylase activity to create variants of an exemplary nucleic acid and test them for the expression of polypeptides having amylase activity.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of amylases to practice the claimed invention. As declared by Dr. Jay Short (see attached Rule 132 declaration), the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for various amylase activities (e.g., alpha amylase), was very high. As declared by Dr. Short, using the teaching of the specification, one skilled in the art could have selected routine methods known in the art at the time of the invention to express variants of nucleic acids encoding the exemplary enzyme of the invention and screen them for expression of polypeptides having various amylase activities. Dr. Short declares that one skilled in the art could have used routine protocols known in the art at the time of the invention, including those described in the instant specification, to screen for nucleic acids encoding polypeptides having a percent sequence identity to SEQ ID NO:125, or active fragments thereof, for various amylase activities. Dr. Short declares that it was routine to screen for multiple substitutions or multiple modifications of an enzyme-encoding sequence and predictably achieve positive results. As declared by Dr. Short, while the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results (i.e., finding variant nucleic acids encoding amylases having various activities) predictable.

Furthermore, Dr. Short declares that it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate

with amylase activity to create variants of the exemplary nucleic acid and test them for the expression of polypeptides or peptides having amylase activity. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including identification of a genus of nucleic acids encoding amylases active under various conditions.

Whether large numbers of compositions (e.g., enzymes, antibodies, nucleic acids, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognize the need to screen numbers of negatives to find a sample that has the desired properties, e.g., amylase-encoding activity. Furthermore, as declared by Dr. Short, the screening procedures used to identify nucleic acids within the scope of the instant invention (e.g., identifying nucleic acids encoding amylase active under various conditions) were all well known

in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the skilled artisan using Applicants' written disclosure could practice the instant claimed invention without undue experimentation.

Accordingly, Applicants respectfully submit that the pending claims meet the written description and enablement requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §102

Claims 1 to 12, 16 to 29, 47, 48, 74 to 86, 89 to 92 and 101 to 106, are rejected under 35 U.S.C. §102, as allegedly anticipated by Tachibana, reference AK.

To address the Examiner's concerns, Applicants have amended the appropriate claims to address this issue. In particular, the lengths of the claimed nucleic acids and the percent sequence identity used to define the claimed genus of nucleic acids have been amended in the appropriate claims. In light of the instant amendment, the rejection under section 102(b) can be properly withdrawn.

Issues under 35 U.S.C. §103

Claims 87 and 88 are rejected under 35 U.S.C. §103, as allegedly unpatentable over Tachibana in view of knowledge one skilled in the art.

As noted above, address the Examiner's concerns, Applicants have amended the appropriate claims to address this issue. In light of the instant amendment, the rejection under section 103(a) can be properly withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, 35 U.S.C. §102, and 35 U.S.C. §103. Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952. Please credit any overpayment to this account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858 720 5133.

Respectfully submitted,

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